

REMARKS

Claims 17, 18, 22, 25, 40-42 and 44 are currently amended. Claim 26 and 38 are canceled. Claims 17, 18, 20, 22-25, 36, 37 and 39-45 are pending. Support for the amendments to the claims is found in the specification as filed. Applicants respectfully submit that the claims, as amended, are in condition for allowance.

Interview Summary and Commonly Assigned TNFSF Applications and Patents

Applicants kindly thank the Examiner for the courtesy of an interview on October 2, 2007. Participants discussed the rejections of record, potential amendments in order to advance prosecution, and the Loetscher reference. Agreement was not reached.

As discussed in the October 2, 2007 Interview, Applicants have filed additional applications on members of the TNFSF:

Application No. 10/338,785, filed January 6, 2003, titled "Novel Variants of RANKL Protein"
Application No. 10/611,363, filed July 1, 2003, titled "Novel Variants of RANKL Protein"
Application No. 10/794,751, filed March 5, 2004, titled "BAFF Variants and Methods Thereof"
Application No. 10/944,473, filed September 16, 2004, titled "BAFF Variants and Methods Thereof"
Application No. 10/820,465, filed March 31, 2004, titled "April Variants and Methods Thereof"
Application No. 10/952,493, filed October 12, 2004, titled "Novel Variants of CD40L Protein"
Application No. 10/963,994, filed October 12, 2004, titled "Protein Based TNF-Alpha Variants for the Treatment of TNF-Alpha Related Disorders"
Application No. 11/108,001, filed April 14, 2005, titled "Protein Based TNF-Alpha Variants for the Treatment of TNF-Alpha Related Disorders"
Application No. 11/472,864, filed June 22, 2006, titled "Pharmaceutical Compositions for the Treatment of TNF-Alpha Related Disorders"
Application No. 11/495,220, filed July 27, 2006, titled "Protein Based TNF-Alpha Variants for the Treatment of TNF-Alpha Related Disorders"
Application No. 11/559,379, filed November 13, 2006, titled "TNF-Alpha Variant Formulations for the Treatment of TNF-Alpha Related Disorders"
Application No. 11/693,318, filed March 29, 2007, titled "TNF-Alpha Variant Formulations for the Treatment of TNF-Alpha Related Disorders"
US Patent 7,244,823, issued July 17, 2007, titled "Protein Based TNF-Alpha Variants for the Treatment of TNF-Alpha Related Disorders"
US Patent 7,144,987, issued December 5, 2006, titled "Protein Based TNF-Alpha Variants for the Treatment of TNF-Alpha Related Disorders"
US Patent 7,056,695, issued June 6, 2006, titled "Novel TNF-Alpha Variants"

Claim Objections

Claim 17 is objected to for a typographical error. Claim 17 has been amended to fix the error.

Claims 17 and 18 are objected to for not defining the acronym TNFSF. The claims have been amended to define the acronym the first time it is used.

Double Patenting

All claims are provisionally rejected for obvious-type double patenting over copending applications Nos. 10/338,083, 10/963,994 and 11/008,091. Terminal disclaims to these applications are filed with the present amendment. Applicants respectfully submit that the currently filed terminal disclaimers renders the double patenting rejection moot.

Claim Rejections – 35 U.S.C. § 112, First Paragraph

Claims 17, 18, 20, 22-26 and 36-45 are rejected under 35 U.S.C. § 112, first paragraph, as not enabling a TNFSF variant protein from interacting with a non-corresponding wild-type TNFSF protein or mixed oligomer thereof. Claims 26 and 38 are cancelled, rendering the rejection as to these claims moot. The independent claims have been amended to clarify that the scope of the claim is only to a variant TNFSF protein interacting with a corresponding wild-type TNFSF protein to form a mixed oligomer. Applicants respectfully submit that the pending claims, as amended, meet all the requirements under 35 U.S.C. § 112, first paragraph, and request this rejection be withdrawn.

Claim Rejections – 35 U.S.C. § 102

Claims 17, 18, 20, 22-26 and 36-45 are rejected under 35 U.S.C. § 102(b) as being anticipated by Loetscher et al., J. Biol. Chem. 1993 Dec., 15:268(35):26350-7. Claims 26 and 38 are cancelled, rendering the rejection as to these claims moot. This reference is the journal publication of US. Patent No. 5,597,899 to Banner, Lesslauer, Loetscher & Stuber ("the '899 Patent"), collectively "Loetscher".

For an anticipation rejection under 35 U.S.C. § 102 to be proper, a single reference must disclose each and every element of a claim. *In re Paulsen*, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); M.P.E.P. § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)).

With respect to the functional limitations, Applicants note that Loetscher attempted to produce TNF- α variants that are fundamentally different from variants of the presently claimed invention. The presently claimed invention is directed to a "variant [TNFSF] protein ... wherein said variant TNFSF protein is capable of interacting with the wild type TNFSF protein to form mixed trimers having at least a 50% decrease in all cognate receptor activation as compared to a homotrimer of said wild-type TNFSF protein." Conversely, Loetscher was attempting to identify human TNF muteins having higher binding affinity for human p75-TNF receptor than for human p55-TNF receptor and to specifically activate the p75 receptor. Moreover, Loetscher was in the context of using a TNF- α variants to kill tumors cells, and thus the variants MUST retain activity to at least one cognate receptor in order to kill tumor cells. This activity is opposite of the activity presently claimed herein. In the instant invention, the variant TNFSF does not activate any cognate receptor; nor does the variant TNFSF member of the present invention have receptor selectivity.

Thus, unlike the instant application, Loetscher is not directed to decreasing receptor activation by TNFSF variants. In fact, to the contrary, Loetscher is directed to increasing the binding affinity of TNF- α

muteins to TNF receptors, in particular the p75-TNF receptor relative to the p55 receptor. Loetscher does not disclose any protein within the scope of the presently claimed invention. In Table 2 at col. 20 and col. 21 of the '899 Patent, Loetscher discloses a select few TNF muteins with multiple substitutions. Of these, muteins L29S-R32W, R31N-R32T, R31N-R32T-N34S and Y87T-E104G do not have "at least one amino acid substitution in the Large Domain, and at least one amino acid in a domain selected from the group consisting of the DE Loop and the Small Domain" as required by the pending claims. Further, double muteins D143V-F144L, D143N-A145R, and D143V-A145S do not have "at least one amino acid substitution in the Large Domain and at least one amino acid substitution in a domain selected from the DE Loop and the Small Domain." Muteins L29S-R32W-S86TI L29S-S86TI R31 E-S86T, R32W-S86T have at least one mutation in the Large Domain and one mutation in the Small Domain, but do not lead to "at least 50% decrease in receptor activation." Instead, Table 2 shows increased function, particularly at receptor p75. Because Loetscher does not teach a variant within the scope of the claims, Loetscher fails to anticipate the presently claimed invention.

Applicants respectfully request the rejection under 35 U.S.C. § 102(b) as being anticipated by Loetscher be withdrawn.

Conclusion

Applicants believe the present application is in condition for allowance. Early favorable communication thereof is respectfully requested. Please direct any calls in connection with this application to the undersigned at (415) 442-1379.

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